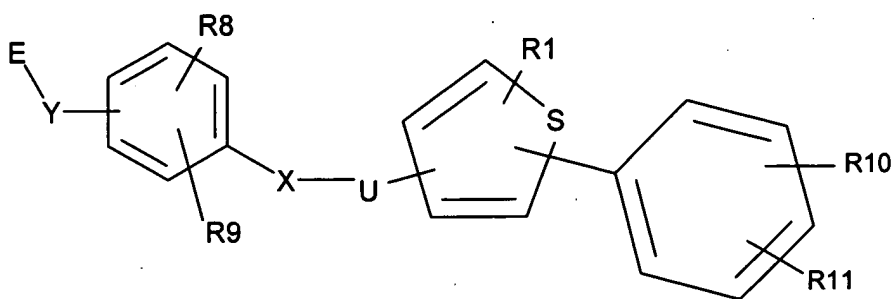


**Amendments to the Claims**

What is claimed is:

1. (Canceled)
2. (Canceled)
3. (Canceled)
4. (Currently Amended) A compound of the Formula I:



or ~~stereoisomers~~ ~~stereoisomers~~, or pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

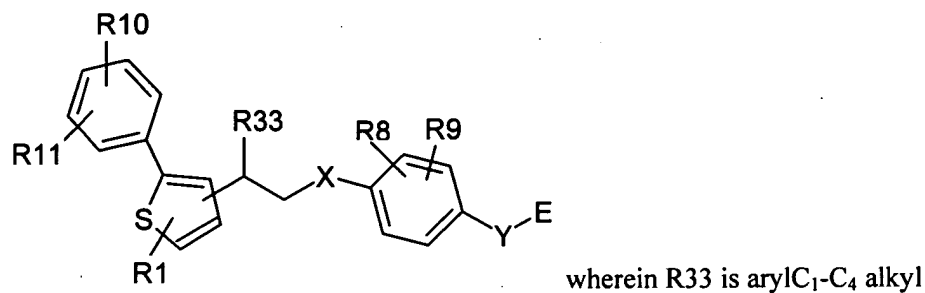
- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, phenyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, wherein C<sub>1</sub>-C<sub>8</sub> alkyl is optionally substituted with from one to three substituents independently selected from R1'; and further wherein C<sub>1</sub>-C<sub>8</sub> alkenyl, phenyl, , and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, are each optionally substituted with from one to three substituents independently selected from R2;
- (b) R1' are each independently selected from the group consisting of hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>1-4</sub>-alkyl, C(O)R<sub>13</sub>, COOR<sub>14</sub>, OC(O)R<sub>15</sub>, OS(O)<sub>2</sub>R<sub>16</sub>, N(R<sub>17</sub>)<sub>2</sub>, NR<sub>18</sub>C(O)R<sub>19</sub>, NR<sub>20</sub>SO<sub>2</sub>R<sub>21</sub>, SR<sub>22</sub>, S(O)R<sub>23</sub>, S(O)<sub>2</sub>R<sub>24</sub>, and S(O)<sub>2</sub>N(R<sub>25</sub>)<sub>2</sub>; R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>24</sub> and R<sub>25</sub> are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;

- (c) R2, R26, R27, R28, and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0-4</sub>-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)<sub>2</sub>R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>;
- (d) X is O;
- (e) U is an aliphatic linker;
- (f) Y is selected from the group consisting of C, O, S, NH and a single bond;
- (g) E is C(R3)(R4)A wherein
  - (i) A is selected from the group consisting of carboxyl, , C<sub>1</sub>-C<sub>6</sub> alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, and acylsulfonamide are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R3 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R4 is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R3 and R4 are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26; with the proviso that when R1 is C<sub>1</sub>-C<sub>8</sub> alkyl, Y is in a para substituted position with relation to X, and X is selected from the group consisting of a bond and O, then R4 is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, and arylC<sub>0</sub>-C<sub>4</sub> alkyl;
- (h) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
- (i) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, , C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

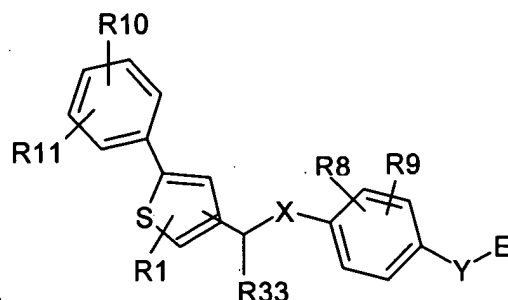
- (j) R10 is selected from the group consisting of C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and aryloxy, provided that when the aliphatic linker, U, is C<sub>1</sub>-C<sub>3</sub> alkyl substituted with arylC<sub>1-4</sub>alkyl, then R10 is selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>'', C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, aryloxy, C(O)R<sub>13</sub>', COOR<sub>14</sub>', OC(O)R<sub>15</sub>', OS(O)<sub>2</sub>R<sub>16</sub>', N(R<sub>17</sub>')<sub>2</sub>, NR<sub>18</sub>'C(O)R<sub>19</sub>', NR<sub>20</sub>'SO<sub>2</sub>R<sub>21</sub>', SR<sub>22</sub>', S(O)R<sub>23</sub>', S(O)<sub>2</sub>R<sub>24</sub>', and S(O)<sub>2</sub>N(R<sub>25</sub>')<sub>2</sub>; and wherein aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three independently selected from R<sub>28</sub>
- (k) R11 is selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>'', C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, aryloxy, C(O)R<sub>13</sub>', COOR<sub>14</sub>', OC(O)R<sub>15</sub>', OS(O)<sub>2</sub>R<sub>16</sub>', N(R<sub>17</sub>')<sub>2</sub>, NR<sub>18</sub>'C(O)R<sub>19</sub>', NR<sub>20</sub>'SO<sub>2</sub>R<sub>21</sub>', SR<sub>22</sub>', S(O)R<sub>23</sub>', S(O)<sub>2</sub>R<sub>24</sub>', and S(O)<sub>2</sub>N(R<sub>25</sub>')<sub>2</sub>; and wherein aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three independently selected from R<sub>28</sub>; and
- (l) R<sub>12</sub>', R<sub>12</sub>'', R<sub>13</sub>', R<sub>14</sub>', R<sub>15</sub>', R<sub>16</sub>', R<sub>17</sub>', R<sub>18</sub>', R<sub>19</sub>', R<sub>20</sub>', R<sub>21</sub>', R<sub>22</sub>', R<sub>23</sub>', R<sub>24</sub>', and R<sub>25</sub>' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl; or the compound of Formula I is selected from the group consisting of 3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid and 3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid.
5. (Canceled)
  6. (Canceled)
  7. (Previously Presented) A compound as claimed by Claim 4 wherein R<sub>4</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, and arylC<sub>0-4</sub> alkyl.
  8. (Previously Presented) A compound as claimed by Claim 4 wherein Y is O.

9. (Previously Presented) A compound as claimed by Claim 7 wherein Y is C.
10. (Previously Presented) A compound as claimed by Claim 7 wherein Y is S.
11. (Canceled).
12. (Currently Amended) A compound as claimed by Claim 4~~Claim 4~~ wherein A is carboxyl.
13. (Previously Presented) A compound as claimed by Claim 4 wherein R1 is H.
14. (Previously Presented) A compound as claimed by Claim 13 wherein A is COOH and R1 is H.
15. (Previously Presented) A compound as claimed by Claim 14 wherein R10 is haloalkyl.
16. (Previously Presented) A compound as claimed by Claim 4 wherein R10 is CF<sub>3</sub>.
17. (Previously Presented) A compound as claimed by Claim 14, wherein R10 is haloalkyloxy.
18. (Previously Presented) A compound as claimed by Claim 4 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sup>12</sup>, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> haloalkyloxy.
19. (Previously Presented) A compound as claimed by Claim 4 wherein R10 is selected from the group consisting of C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and aryloxy.
20. (Previously Presented) A compound as claimed by Claim 4 wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.
21. (Previously Presented) A compound as claimed by Claim 4 wherein R3 and R4 are each independently selected from the group consisting of C<sub>1</sub>-C<sub>2</sub> alkyl.
22. (Previously Presented) A compound as claimed by Claim 4 wherein R3 and R4 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl.
23. (Canceled).
24. (Previously Presented) A compound as claimed by Claim 4 wherein U is C<sub>1</sub>-C<sub>3</sub> alkyl.
25. (Original) A compound as claimed by Claim 24 wherein U is saturated.

26. (Original) A compound as claimed by Claim 24, wherein U is substituted with C<sub>1</sub>-C<sub>3</sub> alkyl.
27. (Original) A compound as claimed by Claim 24, wherein U is substituted with arylC<sub>1</sub>-C<sub>4</sub>alkyl.
28. (Canceled)
29. (Previously Presented) A compound as claimed by Claim 4 wherein R1 is phenyl.
30. (Previously Presented) A compound as claimed by Claim 4 represented by the following Structural Formula II:



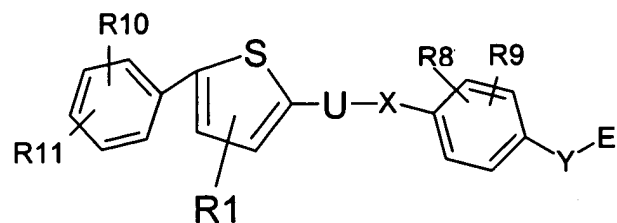
31. (Canceled)
32. (Previously Presented) A compound as claimed by Claim 4 represented by the



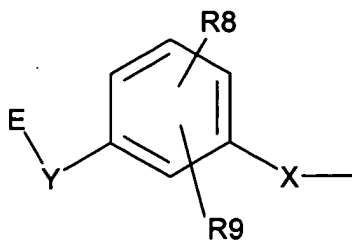
following Structural Formula III:

R33 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, and arylC<sub>0</sub>-C<sub>4</sub> alkyl.

33. (Previously Presented) A compound as claimed by Claim 4 represented by the following Structural Formula IV:



34. (Previously Presented) A compound as claimed by Claim 4 wherein the



headpiece of Formula I is:

35. (Canceled)
36. (Canceled).
37. (Canceled)
38. (Previously Presented) A compound as claimed by Claim 4, wherein the compound is selected from the group consisting of (2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propylsulfanyl}-phenoxy)-acetic acid, (2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propylsulfanyl}-phenoxy)-acetic acid, and 3-(2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propylsulfanyl}-phenyl)-propionic acid.
39. (Previously Presented) A compound as claimed by Claim 4 that is (3-{2-[3-Methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propoxy}-phenyl)-acetic acid.
40. (Previously Presented) A compound as claimed by Claim 4 wherein the compound is selected from the group consisting of

Compound	Name
	<b>3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid</b>
	<b>3-{2-Methyl-4-[3-phenyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid</b>
	<b>3-{4-[3,5-Bis-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-2-methyl-phenyl}-propionic acid.</b>

41. (Previously Presented) A compound as claimed by Claim 4 which is 3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid.
42. (Previously Presented) A compound as claimed by Claim 4 which is the S conformation.
43. (Previously Presented) A compound as claimed by Claim 4 which is the R conformation.
44. (Previously Presented) A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by Claim 4 together with a pharmaceutically acceptable carrier or diluent.
45. (Canceled)
46. (Currently Amended) A method of ~~treating~~ mitigating the progression of the symptoms associated with diabetes mellitus in a mammal, comprising the step

of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound of Claim 4.

47. (Currently Amended) A method of ~~treating~~ mitigating the progression of the symptoms associated with Metabolic syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 4.
48. (Canceled)
49. (Canceled)
50. (Currently Amended) A method of ~~treating~~ mitigating the progression of the symptoms associated with -atherosclerosis in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 4.
51. (Canceled)
52. (Canceled)
53. (Canceled)
54. (Canceled)
55. (Canceled)
56. (Canceled)
57. (Previously Presented) A compound as Claimed by Claim 4 for use as a pharmaceutical.
58. (Previously Presented) A compound as claimed by Claim 4 wherein the compound is radiolabeled.
59. (Canceled)
60. (Canceled)